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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,038	12/22/2000	James J. Benedict	2103.013900	4147

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/748,038	BENEDICT ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2005 and 28 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,8-11,18-21 and 28-30* is/are allowed.

6)☒ Claim(s) *2-7,12-17,22-27 and 31* is/are rejected.

7)☒ Claim(s) *32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050228*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on February 28, 2005 (Information Disclosure Statement) and on June 17, 2005 (amendment and declaration under 37 CFR 1.131) has been entered.

2. The effective filing date of instant claims 1, 11, 21, and 32 is deemed to be October 16, 1998, the filing date of parent application 09/173,989. Instant claims 1, 11, 21, and 32 are deemed to be entitled under 35 U.S.C. 120 to the benefit of the fling date of parent application 09/173,989 because the parent application '989, under the test of 35 U.S.C. 112, first paragraph discloses the claimed invention. Accordingly, Ripamonti et al (U.S. Patent Application Publication 2003/0104977) is not prior art against these claims.

The effective filing date of instant claims 2-10, 12-20, and 22-31 is deemed to be December 22, 2000, the filing date of the instant application. Instant claims 2-10, 12-20, and 22-31 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/173,989 because the parent application '989, under the test of 35 U.S.C. 112, first paragraph does not disclose a mixture of proteins which comprises at least two growth factors selected from those listed in instant claims 2, 12, and 22; does not disclose administration to a human; does not disclose subcutaneous, intramuscular, or intravenous administration; does not disclose discrete or continuous administration; does not disclose administration in combination with a preservative or an adjuvant; does not disclose a mixture of proteins which comprises those

specified in instant claims 8, 18, and 28; does not disclose obtaining the protein mixture by steps including cleaning ground bone, demineralizing cleaned ground bone, and extracting with protein denaturants in general; and does not disclose mammalian bone in general. Accordingly, because U.S. Patent No. 6,211,157 has an earlier effective filing date than these claims and has a different inventive entity than these claims, U.S. Patent No. 6,211,157 is available as prior art against these claims under 35 U.S.C. 102(e). Also, Ripamonti et al (U.S. Patent Application Publication 2003/0104977) is prior art against these claims.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 2, 12, 22, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Ripamonti et al (U.S. Patent Application Publication 2003/0104977). Ripamonti et al teach inducing angiogenesis in mammals by administering a combination of a morphogenic protein and a morphogenic protein stimulator factor. Examples of situations where angiogenesis is required include wound healing, bone repair, ischemic heart disease, and ischemic peripheral vascular disease. The morphogenic protein can be BMP-3,.BMP-4, BMP-5, BMP-6, and BMP-7, and the morphogenic protein stimulatory factor can be TGF-β1, bFGF, IGF-1, EGF, HGF, and TGF-α. See, e.g., the Abstract; paragraph [0003]; Examples 5 and 6; and claims 1, 6, 11, and 13-16. The above-listed morphogenic proteins and morphogenic protein stimulator factors, being identical to those specified in instant claims 2, 12, and 22, are inherently derivable from ground mammalian bone. This rejection assumes that Applicants' claim limitation "derived from ground bone" is a product-by-process limitation which functionally limits the types of proteins

embraced by Applicants' claims, and does not constitute a positive process step which must be practiced in combination with the administering step.

5. Claims 3-7, 13-17, and 23-27 are rejected under 35 U.S.C. 103(a) as being obvious over Ripamonti et al (U.S. Patent Application Publication 2003/0104977). Application of Ripamonti et al is the same as in the above rejection of claims 2, 12, 22, and 31. Ripamonti et al do not teach administration to a human, do not teach administering subcutaneously, intramuscularly, or intravenously, and do not teach administering discretely or continuously. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to induce angiogenesis in humans in the method of Ripamonti et al because Ripamonti et al is not limited to the treatment of any particular patient and because human patients are the most common type of patients in need of angiogenesis. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the active agents of Ripamonti et al subcutaneously, intramuscularly, intravenously, discretely, or continuously, because these are known methods of administration and known dosage schedules in the pharmaceutical arts and it is routine in the pharmaceutical arts to determine all effective and optimal methods of administration and dosage schedules.

6. Applicant's arguments filed June 17, 2005 have been fully considered but they are not persuasive.

The rejections over Ripamonti et al (U.S. Patent Application Publication 2003/0104977) are maintained. The declaration under 37 CFR 1.131 by Akella filed June 17, 2005 is not sufficient to antedate Ripamonti et al (U.S. Patent Application Publication 2003/0104977)

because the declaration is not signed by all of the inventors of the claimed invention. See MPEP 714.04(I). In addition, the following more substantive issues are raised against the declaration:

Section 3 of the declaration refers to "the research agreements presented in Exhibits 1-3"; however, Exhibit 3 is not a research agreement, but rather is a non-prior art publication published in November 2001. The declaration does not contain any assertion as to when the experiments reported in Exhibit 3 were carried out, and accordingly Exhibit 3 does not constitute evidence of conception and/or reduction to practice prior to the filing date of Ripamonti et al.

It is not clear if the declaration contains evidence of reduction to practice prior to the filing date of Ripamonti et al. As quoted in section 4 of the declaration, Exhibit 1, Attachment, IV, Protocol, paragraph 2, Purpose, states "The purpose of this study is to determine whether intramyocardial injections of BP can induce angiogenesis, increase blood flow and improve cardiac function in ischemic myocardium". The use of the word "whether" indicates that the parties to Exhibit 1 did not know what effect BP would have in the tests, i.e. indicates that there was no reduction to practice. Declarant cites to Exhibit 1, Research Agreement Amendment, page 1, paragraph 4.A, as evidence that induction of angiogenesis was successful. However, the cited sentence only discusses proof of safety. Safety is a separate and distinct issue from operability, e.g., a biological agent can be safe yet completely unable to achieve the intended result. The cited sentence is not deemed to constitute evidence of reduction to practice.

Section 5 of the declaration refers to Exhibit 2, Protocol, paragraph 2, Purpose. This paragraph refers to "previous canine studies", and states that one purpose of the proposed study is to "determine the optimal Povidone concentration and molecular weight for delivery of BP via intramyocardial injections in order to induce angiogenesis in the myocardium". However, there

is no discussion in this Exhibit or in the body of the declaration as to what constituted the previous canine studies. The use of the word "optimal" does imply that declarant/inventors had achieved at least some success prior to the Research Agreements. However, if declarant is relying on studies prior to the Research Agreements to establish reduction to practice, then the declaration should explicitly discuss and rely upon those studies, and should provide evidence of those studies in accordance with MPEP 715.07(I), in order to antedate Ripamonti et al.

With respect to sections 7 and 8 of the declaration, as noted above, Exhibit 3 was published in November 2001, and thus is not evidence that the inventors "showed success for a method of promoting natural bypass in a mammal... comprising administering to the mammal a mixture of proteins derived from ground bone... prior to March 31, 2000". Declarant has not stated when the experiments upon which Exhibit 3 is based were carried out.

Given ambiguities in the statements in the exhibits as to whether or not reduction to practice had occurred prior to the filing date of Ripamonti et al, and given the absence of any direct evidence of such reduction, the examiner will not infer that reduction to practice occurred at a date sufficient to antedate Ripamonti et al. A proposed course of experiments as set forth in Exhibits 1 and 2, either alone or in conjunction with a publication dated after the critical reference date, is not sufficient to establish reduction to practice prior to March 31, 2000.

At best, the declaration establishes conception of the invention at some time prior to March 31, 2000 (the filing date of Ripamonti et al) and reduction to practice by November 2001 (the publication date of the Roethy et al article). However, where conception is alleged to occur prior to the critical reference date and reduction to practice is alleged to occur after the critical reference date, the burden lies upon the declarants/inventors to provide evidence of diligence

between conception and reduction to practice. See MPEP 715.07(a). The Akella declaration does not provide any evidence of diligence during the time period outlined above.

7. Claims 1, 8-11, 18-21, and 28-30 are allowed. Claim 32 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

July 14, 2005